

Claims

1. A method for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL in a sample, the method comprising determining the expression level of markers selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1 and/or 2,

wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.1

is indicative for the presence of ball when ball is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.2

is indicative for the presence of cpre when cpre is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 6, 8, 9, 10, 12, 13, 14, 16, 17, 18, 22, 23, 24, 25, 30, 31, 34, 38, 40, 42, 43, 44, 46, 48, and/or 49, of Table 1.3 and/or

a higher expression of at least one polynucleotide defined by any of the numbers 4, 5, 7, 11, 15, 19, 20, 21, 26, 27, 28, 29, 32, 33, 35, 36, 37, 39, 41, 45, 47, and/or 50 of Table 1.3

is indicative for the presence of cpreh when cpreh is distinguished from all other subtypes,

and/or wherein

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a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 17, 18, 19, 20, 21, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 40, 41, 42, 43, 44, 45, 46, 47, and/or 48, of Table 1.4, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 16, 22, 39, 49, and/or 50 of Table 1.4

is indicative for the presence of kort when kort is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.5

is indicative for the presence of pret when pret is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 6, 8, 9, 11, 12, 13, 14, 15, 16, 17, 18, 19, 21, 25, 26, 27, 28, 29, 32, 35, 36, 37, 38, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.6, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 5, 7, 10, 20, 22, 23, 24, 30, 31, 33, 34, and/or 39 of Table 1.6,

is indicative for the presence of prob when prob is distinguished from from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 3, 4, 8, 10, 12, 15, 17, 20, 23, 24, 25, 27, 28, 29, 30, 31, 34, 36, 37, 40, 42, 44, 45, 46, 49, and/or 50 of Table 2.1, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 2, 5, 6, 7, 9, 11, 13, 14, 16, 18, 19, 21, 22, 26, 32, 33, 35, 38, 39, 41, 43, 47, 48,

is indicative for the presence of ball when ball is distinguished from cpre,

and/or wherein

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a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table of Table 2.2, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 26, and/or 37, of Table 2.2

is indicative for the presence of ball when ball is distinguished from cpreph,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 28, 30, 31, 33, 34, 36, 37, 38, 39, 40, 41, 42, 43, 45, 46, 47, 48, and/or 49, of Table 2.3, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 6, 7, 27, 29, 32, 35, 44, and/or 50 of Table 2.3

is indicative for the presence of ball when ball is distinguished from kort,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 3, 5, 6, 7, 13, 17, 18, 19, 21, 22, 26, 27, 30, 32, 34, 36, 38, 40, 47, and/or 48, of Table 2.4, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 4, 8, 9, 10, 11, 12, 14, 15, 16, 20, 23, 24, 25, 28, 29, 31, 33, 35, 37, 39, 41, 42, 43, 44, 45, 46, 49, and/or 50 of Table 2.4

is indicative for the presence of ball when ball is distinguished from pret,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36, 37, 38, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table of Table 2.5, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 29, 30 and/or 39, of Table 2.5,

is indicative for the presence of ball when ball is distinguished from prob,
and/or wherein

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a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 7, 9, 10, 11, 13, 17, 18, 21, 24, 25, 27, 29, 30, 31, 36, 37, 38, 40, 42, 43, 45, 46, 49, and/or 50 of Table 2.6, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 6, 8, 12, 14, 15, 16, 19, 20, 22, 23, 26, 28, 32, 33, 34, 35, 39, 41, 44, 47, and/or 48 of Table 2.6,

is indicative for the presence of cpre when cpre is distinguished from cpreph,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 4, 5, 6, 8, 10, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 27, 28, 29, 30, 31, 32, 35, 36, 38, 40, 41, 43, 44, 45, 46, 48, 49, and/or 50 of Table 2.7, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 3, 7, 9, 11, 22, 26, 33, 34, 37, 39, 42, 47, of Table 2.7,

is indicative for cpre when cpre is distinguished from kort,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 20, 28, 31, 37, 38, and/or 50 of Table 2.8, and/or

a higher expression of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 21, 22, 23, 24, 25, 26, 27, 29, 30, 32, 33, 34, 35, 36, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, and/or 49 of Table 2.8

is indicative for cpre when cpre is distinguished from pret,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 27, 28, 29, 30, 31, 32, 34, 35, 36, 37, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, and/or 50 of Table 2.9,

a higher expression of at least one polynucleotide defined by any of the numbers 26, 33, 41, and/or 49 of Table 2.9

is indicative for cpre when cpre is distinguished from prob,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 3, 6, 12, 17, 23, 28, 34, 35, and/or 41, of Table 2.10, and/or

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a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 4, 5, 7, 8, 9, 10, 11, 13, 14, 15, 16, 18, 19, 20, 21, 22, 24, 25, 26, 27, 29, 30, 31, 32, 33, 36, 37, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.10

is indicative for cpreph when cpreph is distinguished from kort,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 42, and/or 43, of Table 2.11, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.11,

is indicative for cpreph when cpreph is distinguished from pret,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 3, 5, 8, 9, 11, 12, 13, 15, 18, 21, 24, 27, 28, 29, 32, 34, 36, 38, 41, 42, 43, 46, 47, 48, of Table 2.12, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 2, 4, 6, 7, 10, 14, 16, 17, 19, 20, 22, 23, 25, 26, 30, 31, 33, 35, 37, 39, 40, 44, 45, 49, and/or 50 of Table 2.12

is indicative for cpreph when cpreph is distinguished from prob
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 19, and/or 40, of Table 2.13

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.13,

is indicative for kort when kort is distinguished from pret,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 4, 7, 9, 10, 11, 13, 14, 15, 16, 17, 20, 21, 22, 28, 29, 31, 32, 33, 35, 36, 37, 40, 41, 42, 43, 45, 47, 48, and/or 50 of Table 2.14, and/or

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a higher expression of at least one polynucleotide defined by any of the numbers 2, 3, 5, 6, 8, 12, 18, 19, 23, 24, 25, 26, 27, 30, 34, 38, 39, 44, 46, and/or 49, of Tabl 2.14

is indicative for kort when kort is distinguished from prob,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.15,

is indicative for pret when pret is distinguished from prob.

2. The method according to claim 1 wherein the polynucleotide is labelled.
3. The method according to claim 1, wherein the label is a luminescent, preferably a fluorescent label, an enzymatic or a radioactive label.
4. The method according to claim 1, wherein the expression level of at least two, preferably of at least ten, more preferably of at least 25, most preferably of 50 of the markers of at least one of the Tables 1 and/or 2 is determined.
5. The method according to claim 1, wherein the expression level of markers expressed lower in a first subtype than in at least one second subtype, which differs from the first subtype, is at least 5 %, 10% or 20%, more preferred at least 50% or may even be 75% or 100%, i.e. 2-fold lower, preferably at least 10-fold, more preferably at least 50-fold, and most preferably at least 100-fold lower in the first subtype.
6. The method according to claim 1, wherein the expression level of markers expressed higher in a first subtype than in at least one second subtype, which differs from the first subtype, is at least 5 %, 10% or 20%, more preferred at least 50% or may even be 75% or 100%, i.e. 2-fold higher, preferably at least 10-fold, more preferably at least 50-fold, and most preferably at least 100-fold higher in the first subtype.

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7. The method according to claim 1, wherein the sample is from an individual having ALL.

8. The method according to claim 1, wherein at least one polynucleotide is in the form of a transcribed polynucleotide, or a portion thereof.

9. The method according to claim 8, wherein the transcribed polynucleotide is a mRNA or a cDNA.

10. The method according to claim 8, wherein the determining of the expression level comprises hybridizing the transcribed polynucleotide to a complementary polynucleotide, or a portion thereof, under stringent hybridization conditions.

11. The method according to claim 1, wherein at least one polynucleotide is in the form of a polypeptide, or a portion thereof.

12. The method according to claim 8, wherein the determining of the expression level comprises contacting the polynucleotide or the polypeptide with a compound specifically binding to the polynucleotide or the polypeptide.

13. The method according to claim 12, wherein the compound is an antibody, or a fragment thereof.

14. The method according to claim 1, wherein the method is carried out on an array.

15. The method according to claim 1, wherein the method is carried out in a robotics system.

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16. The method according to claim 1, wherein the method is carried out using microfluidics.

17. Use of at least one marker as defined in claim 1, for the manufacturing of a diagnostic for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL.

18. The use according to claim 17 for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL in an individual having ALL.

19. A diagnostic kit containing at least one marker as defined in claim 1, for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL, in combination with suitable auxiliaries.

20. The diagnostic kit according to claim 19, wherein the kit contains a reference for the immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL.

21. The diagnostic kit according to claim 20, wherein the reference is a sample or a data bank.

22. An apparatus for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL,

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Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL in a sample containing a reference data bank.

23. The apparatus according to claim 22, wherein the reference data bank is obtainable by comprising

- (a) compiling a gene expression profile of a patient sample by determining the expression level of at least one marker selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, and/or 2, and
- (b) classifying the gene expression profile by means of a machine learning algorithm.

24. The apparatus according to claim 23, wherein the machine learning algorithm is selected from the group consisting of Weighted Voting, K-Nearest Neighbors, Decision Tree Induction, Support Vector Machines, and Feed-Forward Neural Networks, preferably Support Vector Machines.

25. The apparatus according to claim 22, wherein the apparatus contains a control panel and/or a monitor.

26. A reference data bank for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL obtainable by comprising

- (a) compiling a gene expression profile of a patient sample by determining the expression level of at least one marker selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, and/or 2, and
- (b) classifying the gene expression profile by means of a machine learning algorithm.

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27. The reference data bank according to claim 26, wherein the reference data bank is backed up and/or contained in a computational memory chip.